DETAILED ACTION

Applicant's arguments, filed 06/28/2010, have been fully considered.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have amended their claims, filed 06/28/2010, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Status of Claims

Applicant has newly added claims 34 and 35 in the response filed 06/28/2010, which have been entered and acknowledged. Applicant has cancelled claims 20, 22, and 23.

Claims 1-19, 21, and 24-35 are pending. Claims 1-15 and 27 are withdrawn. Claims 16-19, 21, 24-26, 28-35 are under consideration.

Claim rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
>
> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Claims 16-19, 21, 24-26, 28-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims that depend directly or indirectly from claim 16 and 21 are also rejected due to said dependency.

This rejection is necessitated by amendment.

Claim 16 is directed to a method and recites “directing a mechanical deformation of the target cell using the optical tweezer relative to the auxiliary object, a pushing force or a pulling force of the optical tweezer on the auxiliary object being transferred onto the target cell by the adhered auxiliary object as a one of said induced mechanical forces resulting in said deformation.” This language is confusing for two reasons.

(1) It is unclear what limitation of the claimed method is intended by the phrase "relative to the auxiliary object.” For example, is this referring to a position of the optical tweezer? If so, in what way does this further limit the claimed method? It is unclear.

(2) It is unclear whether the mechanical deformation of the target cell is achieved by the optical tweezer or by the auxiliary object. For example, the phrase “a pulling force or pushing force of the optical tweezer on the auxiliary object being transferred onto the target cell” is confusing. Are the forces "being transferred" directly onto the auxiliary object or the target cell, or otherwise? This rejection could be overcome, for example, by amending the claim to recite "directing a mechanical deformation of the target cell using the optical tweezer, wherein the optical tweezer transfers a pushing force or a

pulling force directly to the auxiliary object adhered to the target cell, and indirectly induces a mechanical deformation of the target cell."

Claim 21 is directed to a system and recites "and wherein a mechanical deformation of the target cell is directed using the optical tweezer relative to the auxiliary object, a pushing force or a pulling force of the optical tweezer on the auxiliary object being transferred onto the target cell by the adhered auxiliary object resulting in said deformation." This limitation appears to be a method step. However, the claimed invention is directed to a system comprising an optical tweezer, microscope, target cell, and auxiliary object. Therefore it is unclear whether applicant intends this limitation to be an active method step or a limitation of the claimed system. If the latter, it is unclear in what way this limitation further limits the claimed system.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, filed 06/28/2010, of the rejection of claims under 35 USC 103 on the basis that Kas and Stromberg do not teach adhering an auxiliary object to a target cell, inducing mechanical forces on the target cell by application of any sort of optical trap to such an auxiliary object, and directing a mechanical deformation of the target cell using the optical tweezer relative to the auxiliary object, a pushing force or a pulling force of the optical tweezer on the auxiliary object being transferred onto the target cell by the adhered auxiliary object as a one of said induced mechanical forces resulting in said deformation are persuasive. Therefore the rejections have been withdrawn. However, these rejections have modified in view of applicant's amendments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16, 19, 21, 24, 25, 26, 28, 30, 32, and 34 are rejected under 35 U.S.C. 103(a) as being made obvious by Kas et al. (US 6,067,859; Issued 30 May 2000), in view of Mammen et al. (Chemistry & Biology, 1996, 3:757-763).

This rejection is necessitated by amendment.

The amended claims are drawn to a method and system for producing optically induced mechanical forces on a target cell that is potentially cancerous. Critical limitations of the claimed method include:

(1) adhering to at least one target cell that is potentially cancerous at least one auxiliary object selected from a group consisting of erythrocytes, hemoglobin, a hemoglobin derivate, a chromophore and a chloroplast;

(2) applying an optical tweezer to said auxiliary object wherein said mechanical forces are induced to said target cell by application of the optical tweezer to said auxiliary object; and

(3) directing a mechanical deformation of the target cell using the optical tweezer relative to the auxiliary object, a pushing force or a pulling force of the optical tweezer on the auxiliary object being transferred onto the target cell by the adhered auxiliary object as a one of said induced mechanical forces resulting in said deformation.

The system comprises an optical tweezer, microscope, target cell, and an adherent object for performing the above method.

For purposes of examination, limitation (3) is interpreted as directing a mechanical deformation of the target cell using the optical tweezer, wherein the optical tweezer transfers a pushing force or a pulling force directly to the auxiliary object adhered to the target cell, and indirectly induces a mechanical deformation of the target cell; see 112 2nd rejection above).

For purposes of applying prior art, the limitation drawn to a target cell that is "potentially cancerous" is broadly interpreted as any cell comprising a nucleus, which satisfies the claim language since any cell with a nucleus is capable of producing genetic mutations or other genetic changes that cause the cell to be cancerous.

Regarding claims 16 and 21, Kas teaches a method and system for optically deforming cells using laser beams [Abstract, Col. 4-5, Summary, Fig. 1, Fig. 2]. The optical system is capable of performing the controlled deformation of biological cells by exposing a cell to two laser beams at an intensity sufficient to deform the cell [See e.g. Col. 3, ¶4, Col. 4, ¶1, Col. 6, and Col. 13, ¶4], wherein gradient forces provided by the beams stretches the cell by pulling the dielectric materials that make up the cell [Col. 7 and 8], which shows applying optical tweezers to an object and inducing forces to mechanically deform a cell by application of optical tweezers, and therefore reads on limitation (2) and limitation (3) in part. Kas teaches optionally measuring the deformation of the cell [Col. 6], wherein the gradient provided by the beams brings about the stretching of the cell as the gradient forces pull the dielectric materials that make up the cell [Col. 7 and 8].Forces can be induced in epithelial cells, eukaryotic cells, melanoma cells, and non-eukaryotic red blood cells [Col. 4-5, Col. 7, lines 20-30, Col. 17, lines 55-65], which teaches the use of a potentially cancerous target cell (e.g. melanoma) and an auxiliary object (e.g. erythrocyte) as in limitation (1).

Regarding claims 19, 24, 25, 26, 28, 30, 32, and 34, the optical system of Kas includes a multiple-beam setup operating at 800 nm [Col. 13, Results], which inherently

teaches long waves, in light of the disclosure regarding "long waves" taught by the instant specification [p.8]. The setup includes beam forming elements, wherein beams are coupled to optical fibers, modulators, lens, and an inverted microscope [See Col. 7, ¶4, and Col. 8 through Col. 9], which shows a laser bean coupled into said beam passage via a lens system. Kas discusses known methods for determining visco-elastics properties of cells using AFM and applies their invention for measuring elasticities of cells [Col. 21], which reads on determining visco-elastic properties of cells.

Kas does not teach adhering at least one auxiliary object to at least one target cell that is potentially cancerous, as in claims 16 and 21.

Kas does not teach directing a mechanical deformation of the target cell using the optical tweezer, wherein the optical tweezer transfers a pushing force or a pulling force directly to the auxiliary object adhered to the target cell, and indirectly induces a mechanical deformation of the target cell, as in claims 16 and 21.

Mammen teaches a method and system for studying collisions between both biological objects and non-biological objects using optical tweezers [See e.g. Abstract, p.761, Col. 2, and Fig. 5]. In particular, Mammen teaches the adhesion of influenza virus-covered spheres to erythrocytes in solution [See e.g. Figures 1, 2, and 3]. The optical tweezers in this case control the position of the erythrocyte and measure the force required to separate erythrocytes from virus-coated microspheres [p.757, Col. 2 and p.758, Col. 2]. Mammen also suggests this method can be applied to other experiments and may complement methods based on deformations of membranes and cell adhesion using optical tweezers [p.760, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have adhered least one auxiliary to at least one target cell that is potentially cancerous, as taught by Mammen, in the method and system of Kas, with a reasonable expectation of success, since Kas teaches the use of erythrocytes and potentially cancerous cells, as set forth above, and since Mammen shows that methods for applying optical tweezers to erythrocytes that have been adhered to virus-covered spheres would have been predictable to one of ordinary skill in the art, as set forth above. The motivation would have been to apply known methods of cell adhesion to investigate collisions of biological particles, such as erythrocytes, bacteria, and viruses, using optical tweezers, as suggested by Mammen [p.760, Col. 2 and p.761, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have directed a mechanical deformation of the target cell using the optical tweezer, wherein the optical tweezer transfers a pushing force or a pulling force directly to the auxiliary object adhered to the target cell, and indirectly induces a mechanical deformation of the target cell, in the method and system made obvious by Kas and Mammen, with a reasonable expectation of success, since Kas shows that the controlled deformation and induction of forces in biological cells using optical tweezers would have been predictable to one of ordinary skill in the art, as set forth above. The motivation would have been to apply known methods of cell adhesion to investigate deformations of biological particles, such as erythrocytes, bacteria, and viruses, using optical tweezers, as suggested by Mammen [p.760, Col. 2 and p.761, Col. 2].

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being made obvious by Kas et al. (US 6,067,859; Issued 30 May 2000), in view of Mammen et al. (Chemistry & Biology, 1996, 3:757-763), as applied to claims 16, 19, 21, 24, 25, 26, 28, 30, 32, and 34, above, and further in view of Nishiguchi et al. (Cell Structure and Function, 1998, Vol. 23, p.143-152).

Kas and Mammen make obvious a method and system for producing optically induced mechanical forces on target cells, as set forth above.

Kas and Mammen do not teach coating an auxiliary object with substances that change surface charge such that the target cell and auxiliary object show surface charges with differing signs, as in claim 17.

Kas and Mammen do not specifically teach the use of fixed erythrocytes, as in claim 18.

Nishiguchi teaches methods for adhering red blood cells using chemicals that change their membrane surface charge [Abstract and p.144, Col. 1, Material and Methods]. RBC are fixed using a particular chemical [p.144, Col. 1, ¶4]. Nishiguchi shows that adhesion between cells is induced by the use of cationic reagents as a result of negatively charged cells surfaces becoming positively charged strength [p.147, Col. 2, and p.148, Col. 1].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have coated erythrocytes with substances that change surface charge such that the target cell and auxiliary object show surface charges with differing

signs, in the method and system made obvious by Kas and Mammen, with a reasonable expectation of success, since Mammen provides known methods for adhering cells using chemicals [p.762, Col. 2, ¶2, ¶3], and since Nishiguchi additionally shows that cationic reagents for adhering erythrocyte cells that effectively change the surface charge of the cells were used with predictable results, as set forth above. The motivation would have been to investigate cell deformation using known chemicals capable of inducing morphological changes in red blood cells, as suggested by Nishiguchi [p.151, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to used fixed erythrocytes, as taught by Nishiguchi, in the method and system made obvious by Kas and Mammen, with a reasonable expectation of success, since Nishiguchi shows that the use of fixed erythrocytes in cell deformation experiments would have been predictable to one of ordinary skill in the art, as set forth above. The motivation would have been to use known and predictable methods of preparing cells for experimentation, as suggested by Nishiguchi [p. 144, Col. 1, and p.151, Col. 2].

Claims 29, 31, 33, and 35 are rejected under 35 U.S.C. 103(a) as being made obvious by Kas et al. (US 6,067,859; Issued 30 May 2000), in view of Mammen et al. (Chemistry & Biology, 1996, 3:757-763), in view of Nishiguchi et al. (Cell Structure and Function, 1998, Vol. 23, p.143-152), as applied to claims 16-19, 21, 24, 25, 26, 28, 30, 32, and 34, above, and further in view of Endlich (2001; IDS filed 5/21/2004).

Kas, Mammen, and Nishiguchi make obvious a method and system for producing optically induced mechanical forces on target cells, as set forth above.

Kas, Mammen, and Nishiguchi do not teach a confocal laser scanning microscope, as in claim 29.

Kas, Mammen, and Nishiguchi do not teach a target cell that is a podocyte, as in claims 31 and 33.

Kas, Mammen, and Nishiguchi do not teach determining activation of a mechano-sensitive ion channel of the target cell resulting in said deformation, as in claim 35.

Endlich teaches methods for applying mechanical stress and strain to podocytes [p.415, Results, Fig. 1, and p.420, Col. 1]. Additionally, Endlich teaches a confocal laser scanning unit [p.414, Col. 2, ¶3]. Endlich also determines deformation of mechano-sensitive cells based on ion channel activation [See e.g. Abstract and p.420, Col. 2]. This system is beneficial for quantifying changes in cytoskeleton response to mechanical stress [p.414, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have used a confocal laser scanning microscope, and a target cell that is a podocyte, in the method and system made obvious by Kas, Mammen, and Nishiguchi, with a reasonable expectation of success, since Endlich shows applying mechanical stress to podocytes (i.e. epithelial cells) and measuring results using a confocal laser with predictable results, as shown above, and since Kas performs

mechanical stress in cells evaluations in cells with predictable results [Col. 4-5, Col. 7, lines 20-30, p.415, Results, Fig. 1, and p.420, Col. 1]. The motivation would have been to better understand the mechano-sensitivity exhibited by podocytes, as suggested by Endlich [p.420, Col. 1], or cytoskeleton function, as suggested by Kas [Col. 5, ¶1].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to have determined the activation of a mechano-sensitive ion channel of the target cell resulting in said deformation, in the method and system made obvious by Kas, Mammen, and Nishiguchi, with a reasonable expectation of success, since Mammen measures deformations of the cytoskeleton, as set forth above, and since Endlich shows that one of ordinary skill in the art would have been able to determine deformation of the cytoskeleton using stretch-activated ion channels with predictable results, as set forth above. The motivation would have been to provide an alternative method of measuring cell deformation, as suggested by Endlich [Abstract].

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached between 12pm-8pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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